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10/573,136

11/06/2006

David Wallach

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08/31/2010

MARSHALL, GERSTEIN & BORUN LLP  
233 SOUTH WACKER DRIVE  
6300 WILLIS TOWER  
CHICAGO, IL 60606-6357

EXAMINER

WEN, SHARON X

ART UNIT

PAPER NUMBER

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/573,136	<b>Applicant(s)</b> WALLACH ET AL.	
	<b>Examiner</b> SHARON WEN	<b>Art Unit</b> 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19, 26-36 and 45-61 is/are pending in the application.
- 4a) Of the above claim(s) 26-36 and 45-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. Applicant's amendment, filed 06/23/2010, has been entered.

Claims 20-25, 37-44 and 62-63 have been canceled.

Claims 1-19, 26-36 and 45-61 are pending.

Claims 26-36 and 45-61 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention/species, there being no allowable generic or linking claim.

Claims 1-19 are currently under examination as they read on an anti-NIK antibody that binds SEQ ID NO: 5, 6, or 3.

2. This Action will be in response to Applicant's Arguments/Remarks, filed 06/23/2010.

The rejections of record can be found in the previous Office Action, mailed 12/23/2009.

New Grounds of rejection necessitated this Office Action being Non-Final.

***Claim Rejections - 35 USC § 112 second paragraph***

3. The previous claim rejection under 35 USC 112 second paragraph has been withdrawn in view of Applicant's amendment, filed 06/23/2010.

***Claim Rejections - 35 USC § 112 first paragraph***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The previous scope of enablement rejection for the recitation of "a CDR" in claims 5 and 18 been withdrawn in view of Applicant's amendment, filed 06/23/2010. Furthermore, Applicant's assurance that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the

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granting of a patent in U.S. patent applications in the remarks, filed 06/23/2010, has obviated the previous rejection for a biological deposit.

6. Applicant's amendment, changing "an amino acid sequence" to "the amino acid sequence" and deletion of "a portion thereof" have obviated part of the rejection. However, given that claim 12 still recites "**a mutein, functional derivative, active fraction, circularly permuted derivative or a salt thereof**", the following rejection is set forth:

7. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds the amino acid sequence set forth in SEQ ID NO: 5, 6 or 3, does not reasonably provide enablement for an antibody that binds **a mutein, functional derivative, active fraction, circularly permuted derivative or a salt of NIK**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Under the broadest reasonable interpretation, the present claims are broadly drawn to antibodies that bind to variants of NIK that comprise phosphorylated T559 residue. However, other than the antibodies binding to the amino acid sequence set forth in SEQ ID NOs: 5, 6 or 3, there does not appear to be an actual reduction to practice of an antibody that binds other species of the genus encompassing the variants of NIK; nor is there a complete or partial structure of an antibody capable of binding all the species of the above mentioned genus in detailed drawing or through a structural chemical formula, e.g., sequence of the antibody.

Furthermore, a skilled artisan is well aware that such antibodies binding the amino acid sequences of SEQ ID NOs: 5, 6 or 3 would not reasonably be expected to be reactive with all members of the genus encompassing all the variants of the peptides. For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclosed that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214,

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1980; see entire document) disclosed that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Moreover, for instance, Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

Give that the instant specification disclosed that the claimed antibody is used for detection of NIK, one of skill in the art would not be able to use the antibody that binds to the variants of NIK such as a mutein, functional derivative, active fraction, circularly permuted derivative or salt thereof to detect NIK commensurate in scope with the instant disclosure because, as the state of the art discussed above, the antibody that binds the variants of NIK would not be expected to have the antigen-specificity for NIK.

Therefore, the specification, as-filed, provided insufficient guidance to lead a person of skill in the art to make or use all the antibodies that bind muteins, functional derivatives, active fractions, circularly permuted derivatives or salts of NIK to detect NIK commensurate in scope of the instant disclosure.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

In response to Applicant's argument that one of ordinary skill in the art would have the requisite skill to generate anti-NIK antibodies having in hand the NIK peptides encoded by the amino acid sequences recited in the claims using the specification as a

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guide, it is noted that the issue there is that one of skill in the art would not be able to make or use an antibody raised against SEQ ID NO: 5 that would have the specificity to detect all muteins, functional derivatives, active fractions, circularly permuted derivatives or salts of NIK because an antibody that binds SEQ ID NO: 5 would not necessarily have the specificity for all muteins, functional derivatives, active fractions, circularly permuted derivatives or salts of NIK. The binding of antibody to antigen is highly specific as discussed in the previous Office Action (see above for Lederman et al., Li et al., and Houghten et al.). The present claims recite "*a portion of said amino acid sequence*" and require the antibody to be capable of detecting NIK in a Western blot, ELISA or immunoprecipitation assay. "*A portion of the amino acid sequence*" reads on any fragment of the amino acid sequence and encompasses as few as one amino acid. Given the unpredictability in the art pertaining to changing sequence in the antigen and retaining antibody binding capability as taught by Lederman et al., Li et al., and Houghten et al., and in view of lack of teaching by the instant specification on making or using an antibody that binds to sequences other than the full length SEQ ID NO: 5, one of skill in the art would not be able to make or use antibodies that binds to as few as one amino acid of SEQ ID NO: 5 and retain its binding capacity to NIK in order to detect NIK in Western, ELISA or immunoprecipitation assay without undue experimentation. Similarly, antibodies that bind specifically to SEQ ID NO: 5 would not be able to bind all the muteins, functional derivative, active fraction, circularly permuted derivative or salt of NIK because these variants of NIK represent a genus encompassing different amino acid sequences.

Applicant's argument has not been found convincing. Therefore, this rejection is maintained as it applies to amended claims.

*New Grounds of rejection are set forth below:*

8. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for the all muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK as targets of the claimed antibodies because there is a lack of sufficient written description to support the recited genus of the antibody targets.

The standard for Written Description is met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." See *Enzo Biochem., Inc. v. Gen-Probe Incorporated* 323 F.3d 956 (Fed. Cir. 2002).

The instant specification disclosed that the polypeptide set forth in SEQ ID NO: 3, 5 and 6 are epitopes to which anti-NIK antibodies. However, the present claims are drawn to a genus of the antibody targets that encompasses any muteins, functional derivatives, active fractions, circularly permuted derivatives or salts of NIK.

The fact that two polypeptides that are homologous in structure or share certain degrees of identity in sequence does not in and of itself required that the two sequences share any functional activity such as anti-microbial activity. In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK as targets of the claimed antibodies.

A person of skill is well aware, at the time of the invention was made, that different molecules, even with sequence similarity, do not necessarily have the same function. For example, Attwood (Science 290: 471-473, 2000) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of

similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 18: 34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Therefore, the disclosed amino acid sequences set forth in SEQ ID NOs: 3, 5 and 6 are not sufficiently representative of the genus encompassing all muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK as targets of the claimed antibodies because the disclosure fails to describe the common attributes or characteristics that identify all members of the genus, known and unknown at the time the invention was made.

As the fragments and variants of NIK are the targets of the recited antibody, Applicant has not provided a sufficient written description of all the antibodies that are capable of binding to all the targets for the following reasons.

Other than the antibody binding to the SEQ ID NO: 3, 5 and 6, there does not appear to be an actual reduction to practice of an antibody that binds other species of the genus encompassing all the muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK; nor is there a complete or partial structure of an antibody capable of binding all the species of the above mentioned genus in detailed drawing or through a structural chemical formula, e.g., sequence of the antibody.

Furthermore, a skilled artisan is well aware that such antibodies binding SEQ ID NO: 3, 5 or 6 would not reasonably be expected to be reactive with all the muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclosed that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214,



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1980; see entire document) disclosed that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Moreover, for instance, Houghten et al. (New Approaches to Immunization, Vaccines 86, Cold Spring Harbor Laboratory, p. 21-25, 1986) taught the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten et al. state (see page 24): "One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool."

Therefore, the specification does not provide for sufficient written description to reasonably convey to one skilled in the relevant art that, at the time the application was filed, Applicant had possession of all antibodies capable of binding to all the muteins, functional derivatives, active fractions, circularly permuted derivatives, salts of NIK.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-4, 6-10, 12, 14-16 and 19 stand rejected under 35 U.S.C. 102(e) as being anticipated by Schreiber et al. (US 6,822,138 B1, see entire document).

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated herein for Applicant's convenience.

Schreiber taught a polyclonal antibody that binds specifically to NIK (see e.g., column 15, paragraph 4) and a pharmaceutical composition comprising the antibody as a modulator of NIK and a pharmaceutically acceptable carrier (see column 18, lines 41-49 and column 27, lines 32-43).

Although Schreiber et al. did not teach the polyclonal antibody to NIK to bind specifically to a portion of NIK comprising phosphorylated threonine 559, given that polyclonal antibodies are known to bind multiple epitopes on one antigen, the prior art polyclonal antibody raised against NIK would necessarily bind to the epitopes comprising threonine 559. Therefore, the prior art antibody would be capable of specifically detecting phosphorylated NIK or a specific portion thereof by Western, ELISA or immunoprecipitation. Furthermore, the prior art antibody would also be able to regulate a biochemical activity of NIK because it is a polyclonal antibody that binds multiple epitopes on NIK which would be the kinase activation site of NIK, thereby inhibiting the activity of NIK.

Since the Office does not have a laboratory to test the prior art polyclonal antibody, it is Applicant's burden to provide objective evidence showing that Schreiber's polyclonal antibody raised against NIK does not bind to portions of NIK comprising phosphorylated threonine 559.

Applicant argues that Schreiber's polyclonal antibody does not anticipate the present claims because not all polyclonal anti-NIK antibodies specifically bind the phosphorylated version of NIK. Applicant relies on the instant specification for support of this argument by pointing to Examples 1 and 2. In response, it is noted that the

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claims are drawn to any polyclonal antibody that binds SEQ ID NO: 5, 6 or 3 wherein the sequence comprising phosphorylated T559. It does not require the antibody to bind to a specific epitope that contains phosphorylated T559 but only that the sequence has to have phosphorylated T559 residue. As SEQ ID NO: 5 is a 947-amino-acid-long polypeptide, a polyclonal antibody that binds NIK would bind to some epitopes in SEQ ID NO: 5. Therefore, Applicant's argument has not been found convincing. The rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-10, 12, 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schreiber et al. (US 6,822,138 B1) in view of Lin et al. (Mol Cell Biol. 1998, 18(10):5899-5907) and Campbell (*Monoclonal Antibody Technology*, 1984, Chapter 1, pages 1-32), Green (*JIM* 1999 231:11-23) and Owens et al. (*JIM*, 1994, 168:149-165).

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated herein for Applicant's convenience.

The teaching by Schreiber et al. has been discussed supra.

Schreiber et al. did not teach the antibody to bind specifically to the portion of NIK comprising a phosphorylated threonine 559 as set forth in SEQ ID NO: 6 or 3. However, it would have been obvious to one of ordinary skill in the art, at the time of the invention was made, to make an antibody specifically to the region comprising phosphorylated threonine 559 because the region containing threonine 559 was known to be the activation loop of NIK as taught by Lin et al. (see entire document). In particular, Lin taught that substitution of Thr-559 with an alanine within the activation loop abolishes NIK activity and its ability to phosphorylate and activate IKK $\alpha$ ; and that a NIK-T559A mutant also dominantly interferes with TNF- $\alpha$  induction of NF- $\kappa$ B (see e.g., Results and Discussion). Given such knowledge, one of ordinary skill in the art would have been

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reasonably expected to make an antibody that would bind to a region containing Thr-559 in the activation loop to block the site for activation. Furthermore, one of ordinary skill in the art would have been motivated to make such antibody in view of Campbell's teaching in that it is customary for any group working on a macromolecule to make monoclonal antibodies to it, sometimes even without a clear objective for their application (see Campbell, page 29, last paragraph). Given that Lin et al. taught that the activation loop of the NIK contained Thr-559 and that the phosphorylation of Thr-559 is critical in the regulation of NIK function (see Introduction), one of ordinary skill in the art would have been motivated to make an antibody against the activation loop of the NIK which contains the phosphorylated Thr-559 to study the molecule using common assays such as Western, ELISA and immunoprecipitation.

*With respect to "human antibody", the following is noted.*

Schreiber et al. did not teach that the anti-NIK antibody is a human antibody. However it have been obvious to one of skill in the art at the time of the invention was made to make a human antibody against NIK because it was well-known in the art to make a human antibody as evidenced by Green (see entire document).

In particular, Green taught that XenoMouse strains of mice produced human monoclonal IgG antibodies (see, e.g., page 13-16, Section 2). Furthermore, Green taught that immunization of XenoMouse mice with human antigen *routinely* results in a robust secondary immune response, which can be ultimately captured as a large panel of antigen-specific fully human IgG mAb of sub-nanomolar affinity (see, e.g., Abstract). More over, one of ordinary skill in the art would also have been motivated to make the human anti-NIK antibodies because Green taught that monoclonal antibodies from XenoMouse animals have been shown to have therapeutic potential both in vitro and vivo (see, e.g., Abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to make the human anti-NIK antibody given that both the starting material, NIK antigen and the method of making human antibody with the antigen were both well-known in the art at the time of the invention was made.

*With regard to "humanized or chimeric antibody or antibody fragments", the following is noted.*

Although Schreiber did not teach the antibody to be humanized or chimeric, it would have been obvious to one of ordinary skill in the art at the time of the invention was made to generate a chimeric or humanized antibody against NIK because it is well-known in the art to make chimeric or humanized antibodies as evidenced by Owens et al. (see entire document, in particular, see pages 150-155).

In particular, Owens et al. taught the methods of humanizing rodent monoclonal antibodies by making human chimeric and human CDR-grafted

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antibodies from rodent monoclonal antibodies (see pages 150-155). Furthermore, Owen also taught the construction of antibody fragments such as Fv and scFv (see page 155).

One of ordinary skill in the art would have been motivated to make a chimeric or humanized antibody against NIK and the antibody fragments as taught by Schreiber et al. because antibodies can be used for therapeutic purposes and that making a rodent monoclonal antibody chimeric or humanized is advantageous to the rodent monoclonal antibody for human diagnosis or therapy as taught by Owens (see Introduction). Moreover, using antibody fragment has the advantage of faster clearance from the body. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to make an antibody that binds and antagonizes NIK wherein the antibody is chimeric or humanized, as well as an antibody fragment.

Given the above discussion, the invention, as a whole, was *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's argument and Examiner's rebuttal are essentially the same as above. Applicant argues that it is unpredictable to make an antibody specific to make an antibody that specifically binds NIK comprising phosphorylated T559 because not all polyclonal anti-NIK antibodies specifically bind the phosphorylated version of NIK. Applicant relies on the instant specification for support of this argument by pointing to Examples 1 and 2. In response, it is noted that the claims are drawn to any polyclonal antibody that binds SEQ ID NO: 5, 6 or 3 wherein the sequence comprising phosphorylated T559. It does not require the antibody to bind to a specific epitope that contains phosphorylated T559 but only that the sequence has to have the phosphorylated T559 residue. As SEQ ID NO: 5 is a 947-amino-acid-long polypeptide, a polyclonal antibody that binds NIK would bind to some epitopes in SEQ ID NO: 5. Moreover, given that phosphorylated T559 was known in the art at the time of the invention was made, it would have been within the ordinary artisan's technical grasp to raise an antibody against a portion of NIK that contains phosphorylated T559 and test the specificity of the antibody. Therefore, Applicant's argument has not been found convincing. The rejection is maintained.

***Conclusion***

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571)272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/  
Examiner, Art Unit 1644  
August 29, 2010